

Psychiatric Briefs

Sustained-Release Bupropion for Smoking Cessation in African Americans: A Randomized Controlled Trial

Ahluwalia JS, Harris KJ, Catley D, et al.

Background: Although African Americans experience high morbidity and mortality attributable to smoking and have smoking and quitting patterns different from those of other groups, few clinical trials for smoking cessation have been conducted in African Americans. This study compared bupropion sustained release (bupropion SR) with placebo for smoking cessation among African Americans. **Method:** Volunteers who smoked > 10 cigarettes per day were recruited by target media and health care professionals. A total of 600 African American adults treated at a community-based health care center were included in this randomized, double-blind, placebo-controlled trial conducted from February 11, 1999, to December 8, 2000. Participants were randomly assigned to 7 weeks of twice-daily treatment with either 150 mg of bupropion SR (N = 300) or placebo (N = 300). Brief motivational counseling was provided in person at baseline, quit day, weeks 1 and 3, and end of treatment (week 6) and by telephone at day 3 and weeks 5 and 7. Biochemically confirmed 7-day point prevalence abstinence at weeks 6 and 26 following quit day was the chief outcome measure. **Results:** At the end of 7 weeks of treatment, the confirmed abstinence rates were 36.0% with bupropion SR and 19.0% with placebo (intent-to-treat analysis; 17.0 percentage point difference; 95% CI = 9.7 to 24.4; $p < .001$). Abstinence rates at 26 weeks were 21.0% with bupropion SR and 13.7% with placebo (7.3 percentage point difference; 95% CI = 1.0 to 13.7; $p = .02$). A greater mean \pm SD reduction in depression symptoms at week 6 was experienced by subjects receiving bupropion SR (2.96 ± 9.45) than by those receiving placebo (1.13 ± 8.84), and after continuous abstinence was controlled for, bupropion SR-treated subjects gained less weight than those receiving placebo. **Conclusions:** Bupropion SR was effective in helping African Americans quit smoking and may be an aid in reducing smoking-attributable health disparities.

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Citalopram Treatment of Compulsive Shopping: An Open-Label Study

Koran LM, Bullock KD, Hartston HJ, et al.

Background: Compulsive shopping, a DSM-IV impulse-control disorder not otherwise specified, is characterized by preoccupation with shopping and inability to resist buying unneeded items, with resulting marked distress, social or occupational impairment, and financial and/or familial problems. Because an open-label trial suggested that fluvoxamine, a selective serotonin reuptake inhibitor (SSRI), is effective for this dis-

order, we tested the effectiveness of the SSRI citalopram.

Method: We enrolled adults meeting formal diagnostic criteria (as defined by McElroy and colleagues) in a 12-week open-label trial. We excluded subjects with obsessive-compulsive disorder, bipolar disorder, substance abuse or dependence, or psychotic disorders. Citalopram treatment was begun at 20 mg/day and increased every 2 weeks by 20 mg/day, absent marked response and limiting side effects, to 60 mg/day. At endpoint, all subjects were asked to give written informed consent for follow-up telephone interviews at 3-month intervals for 12 months. **Results:** We enrolled 24 subjects, 22 women and 2 men, whose mean \pm SD age was 43.7 ± 8.1 years; most had been shopping compulsively for 2 decades or more. Citalopram (mean \pm SD endpoint dose = 35.4 ± 21.4 mg/day) produced rapid, marked, sustained improvements on both the Yale-Brown Obsessive Compulsive Scale–Shopping Version and the Clinical Global Impressions-Improvement (CGI-I) scale in subjects with and without comorbid conditions. Seventeen subjects (71%) were responders, achieving ratings of much or very much improved on the CGI-I, including 2 of the 3 subjects who discontinued for adverse events (sedation or agitation). During a 6-month follow-up period, those continuing citalopram therapy were less likely to relapse than those discontinuing the medication. **Conclusion:** Citalopram appears to be a safe and effective treatment for compulsive shopping. Acute and long-term, double-blind, placebo-controlled trials of citalopram and other SSRIs for the treatment of this disorder are indicated.

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Toward a Comprehensive Developmental Model for Major Depression in Women

Kendler KS, Gardner CO, Prescott CA

Objective: An individual's probability of suffering from an episode of major depression is influenced by several etiologic factors that are interrelated through developmental pathways. The authors generated a developmental model for the etiology of major depression in women by means of structural equation modeling. **Method:** Using data from 1942 adult female twins who were interviewed up to 4 times over a 9-year period, the authors constructed a developmental model to predict depressive episodes in the year before the most recent interview. A total of 18 risk factors from 5 developmental tiers were considered: (1) childhood (genetic risk, disturbed family environment, childhood sexual abuse, and childhood parental loss), (2) early adolescence (neuroticism, self-esteem, and early-onset anxiety and conduct disorder), (3) late adolescence (educational attainment, lifetime traumas, social support, and substance misuse), (4) adulthood (history of divorce and past history of major depression), and (5) the past year (marital problems, difficulties,

and stressful life events that were either dependent on or independent of the respondent's own behavior). **Results:** The best fitting model, accounting for 52% of the variance in liability to major depression in the last year, included 6 correlations and 64 paths and provided an excellent fit to the data. The findings suggest that 3 broad pathways—reflecting internalizing symptoms, externalizing symptoms, and psychosocial adversity—lead to the development of risk for major depression in women. **Conclusions:** Because major depression is etiologically complex, consideration of a broad array of risk factors from multiple domains will be needed to fully understand the disorder. Problems with causal interference, retrospective recall bias, and limitations associated with a purely additive statistical model necessitate that these results, although plausible, be treated with caution.

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Medical Morbidity, Mental Illness, and Substance Use Disorders

Dickey B, Normand S-LT, Weiss RD, et al.

Background: Although studies have generally shown that medical disorders are more prevalent in individuals with mental illness, such research did not take into account comorbid substance use disorders. This study sought to determine whether certain medical disorders are more prevalent in severely mentally ill adults and whether the prevalence of these medical illnesses is increased when comorbid substance use disorders are present. **Method:** A cross-sectional observational study design was used to analyze administrative data from the Massachusetts Division of Medical Assistance. Of the sample of 26,332 Medicaid beneficiaries aged 18 to 64 years, 11,185 had received treatment for severe mental illness. Twelve-month prevalence rates were computed, and the effect of a substance use disorder or another mental illness on the risk of having a medical disorder was estimated using logistic regression. **Results:** Medicaid beneficiaries with severe mental illness had a significantly higher age- and gender-adjusted risk of medical disorders considered in the study ($p = .001$) than did beneficiaries not treated for severe mental illness. Individuals with a comorbid substance use disorder had the highest risk for 5 of the disorders considered. **Conclusions:** Three implications follow from the higher treated prevalence of certain medical disorders among adults with severe mental illness: substance use disorder is an important risk factor and necessitates early detection; high priority should be given to integrating the treatment of severe mental illness and medical disorders; and specialized disease self-management techniques should be developed.

(*Psychiatr Serv* 2002;53:861–867)

Combining Antidepressants for Treatment-Resistant Depression: A Review

Lam RW, Wan DDC, Cohen NL, et al.

Objective: Many patients with depression remain poorly responsive to antidepressant monotherapy. One approach for managing treatment-resistant depression is to combine antidepressants and

to capitalize on multiple therapeutic mechanisms of action. This review critically evaluates the evidence for efficacy of combining antidepressants. **Method:** A MEDLINE search of the last 15 years (up to June 2001), supplemented by a review of bibliographies, was conducted to identify relevant studies. Criteria used to select studies included (1) published studies with original data in peer-reviewed journals, (2) diagnosis of depression with partial or no response to standard treatments, (3) any combination of 2 antidepressants with both agents used to enhance antidepressant response, (4) outcome measurement of clinical response, and (5) sample size of 4 or more subjects. **Results:** Twenty-seven studies (total $N = 667$) met the inclusion criteria, including 5 randomized controlled trials and 22 open-label trials. In the 24 studies (total $N = 601$) reporting response rates, the overall mean response rate was 62.2%. Methodological limitations included variability in definitions of treatment-resistant depression and response to treatment, dosing of medications, and reporting of adverse events. **Conclusion:** There is limited evidence, mostly in uncontrolled studies, supporting the efficacy of combination antidepressant treatment. Further randomized controlled trials with larger sample sizes are required to demonstrate the efficacy of a combination antidepressant strategy for patients with treatment-resistant depression.

(*J Clin Psychiatry* 2002;63:685–693)

Cigarette Smoking and Panic: The Role of Neuroticism

Goodwin R, Hamilton SP

Objective: The current study was undertaken to investigate whether neuroticism is associated with a higher risk of the co-occurrence of cigarette smoking and panic attacks. **Method:** Data were taken from a representative household survey of the adult population of the United States (Midlife Development in the United States Survey; $N = 3032$). The association between cigarette smoking and panic attacks and whether neuroticism was an independent predictor of the co-occurrence of cigarette smoking and panic attacks were determined using multivariate logistic regression analyses. **Results:** Of the individuals who had a history of panic attacks, most (81.1%) had been regular smokers at some point during their lifetime; the percentage of regular smokers was significantly higher in those experiencing panic attacks than in the group of individuals without a history of panic attacks (69.4%; $\chi^2 = 9.0$, $df = 1$, $p = .002$). Regular cigarette smoking was associated with a significantly greater risk of current panic attacks (odds ratio = 1.9, 95% CI = 1.3 to 2.9). This significant association remained after controlling for demographic variables, depression, and alcohol/substance use disorders; it did not, however, persist after analyses adjusted for neuroticism, which independently predicted the co-occurrence of panic attacks and regular cigarette smoking but did not predict either in the absence of the other. **Conclusions:** These findings, consistent with previous research, suggest that panic attacks are associated with a higher risk of cigarette smoking. The findings also provide new evidence that neuroticism may play a vital role in the relationship between panic attacks and

cigarette smoking. Although these data are preliminary, they suggest, if they are replicated, that a shared vulnerability for the co-occurrence of panic attacks and cigarette smoking may be reflected by neuroticism. Future study is needed to determine the mechanism of this association.

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Alternative Treatments for Depression: Empirical Support and Relevance to Women

Manber R, Allen JJB, Morris MM

Background: This article is a critical review of the efficacy of selected alternative treatments for unipolar depression including exercise, stress management techniques, acupuncture, St. John's wort, bright light, and sleep deprivation. Issues related to women across the life span, including pregnancy and lactation, are highlighted. **Data Sources:** Evidence of efficacy is based on randomized controlled trials. A distinction is made between studies that address depressive symptoms and studies that address depressive disorders. The review emphasizes issues related to effectiveness, such as treatment availability, acceptability, safety, and cost and issues relevant to women. **Data Synthesis:** Exercise, stress reduction methods, bright light exposure, and sleep deprivation hold greater promise as adjuncts to conventional treatment than as monotherapies for major depression. The evidence to date is not sufficiently compelling to suggest the use of St. John's wort in favor of or as an alternative to existing U.S. Food and Drug Administration–regulated compounds. Initial evidence suggests that acupuncture might be an effective alternative monotherapy for major depression, single episode. **Conclusion:** This review indicates that some unconventional treatments hold promise as alternative or complementary treatments for unipolar depression in women and have the potential to contribute to its long-term management. Additional research is needed before further recommendations can be made, and there is an urgent need to carefully document and report the frequency of minor and major side effects.

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The Natural History of Late-Life Depression: A 6-Year Prospective Study in the Community

Beekman ATF, Geerlings SW, Deeg DJH, et al.

Background: Depression in later life is common and has consequences for well-being, daily functioning, mortality, and service utilization. Frequent observation over time is required to accurately assess the natural history of late-life depression, which more often manifests as subthreshold disorders than as disorders meeting rigorous diagnostic criteria. Observing the natural history of late-life depression in the community, with a systematic comparison of the prognosis of those who did and did not fulfill rigorous diagnostic criteria for depressive disorders, was the primary aim of this study. **Method:** A large cohort of depressed elderly individuals (N = 277) from within the Longitu-

dinal Aging Study Amsterdam was identified and followed up using 14 observations over 6 years. Self-reports (Center for Epidemiological Studies Depression Scale [CES-D]) and diagnostic interviews (Diagnostic Interview Schedule) were used to measure depression. In addition, natural history was studied for severity (CES-D score) and duration of symptoms, type of clinical course, and stability of diagnoses. **Results:** The mean (SD) CES-D score during the 6-year follow-up period was 17.28 (6.61), which was above the 85th percentile of the population average. Only 14% of subjects had symptoms that were short-lived. Remission occurred in 23% of subjects, an unfavorable but fluctuating course was seen in 44%, and a severe chronic course was observed in 32%. A clear gradient was seen in which subthreshold disorders were associated with the best outcome, followed by major depressive disorder, dysthymic disorder, and double depression. Still, the presence of subthreshold disorders usually portended unfavorable prognoses, and those with subthreshold depression had a high risk of developing DSM affective disorders. **Conclusions:** Late-life depression in the community has a poor natural history. Although DSM disorders are rare among elderly persons, they do identify those with the worst prognosis. Subthreshold depression is itself often a serious and chronic condition.

(*Arch Gen Psychiatry* 2002;59:605–611)

Nonpsychiatric Illness Among Primary Care Patients With Trauma Histories and Posttraumatic Stress Disorder

Weisberg RB, Bruce SE, Machan JT, et al.

Background: Research suggests that individuals with a history of trauma or who have symptoms of posttraumatic stress disorder (PTSD) have a greater risk of developing medical illnesses. This study examined the relationship between PTSD, trauma, and nonpsychiatric medical conditions. **Method:** Comorbid psychiatric and substance abuse problems and history of trauma were assessed in 502 primary care patients with at least one DSM-IV anxiety disorder. Patients also completed a self-report assessment of current and lifetime medical conditions, lifetime use of tobacco, and current regular exercise. **Results:** No history of trauma was found in 84 patients (17%), history of trauma without PTSD was found in 233 patients (46%), and PTSD was found in 185 (37%). A significantly greater number of current and lifetime medical conditions ($p < .001$) were reported by patients with PTSD than by those with anxiety disorders but without PTSD. A number of specific medical problems were more likely in patients with PTSD, including anemia, arthritis, asthma, back pain, diabetes, eczema, kidney disease, lung disease, and ulcer. Several variables possibly accounting for the greater likelihood of comorbid medical illnesses in patients with PTSD were examined in a logistic regression analysis; PTSD itself was found to more strongly predict reported number of medical problems than did trauma history, physical injury, lifestyle factors, or comorbid depression. **Conclusions:** PTSD may be associated with a higher rate of general medical complaints.

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Lithium and Valproate Treatment of Pathological Gambling: A Randomized Single-Blind Study

Pallanti S, Quercioli L, Sood E, et al.

Objective: The aim of the present study was to evaluate the efficacy and safety of lithium and valproate in nonbipolar pathological gamblers. **Method:** Forty-two subjects with DSM-IV–defined pathological gambling entered a 14-week single-blind trial with lithium (N = 23) or valproate (N = 19). A total of 15 subjects on lithium treatment and 16 patients on valproate treatment completed the 14-week protocol. **Results:** At the end of the 14-week treatment period, both the lithium and the valproate groups showed significant ($p < .01$) improvement in mean score on the Yale-Brown Obsessive Compulsive Scale modified for pathological gambling. This improvement did not significantly differ between groups. Fourteen (60.9%) of the 23 patients taking lithium and 13 (68.4%) of the 19 patients taking valproate were responders based on a Clinical Global Impressions-Improvement score of much or very much improved. **Conclusion:** Findings from the present study suggest the efficacy of both lithium carbonate and valproate in the treatment of pathological gambling. This is the first controlled trial of the efficacy of mood stabilizers in pathological gambling. A double-blind, placebo-controlled trial is required to confirm these findings.

(*J Clin Psychiatry* 2002;63:559–564)

Psychological Reactions to Terrorist Attacks: Findings From the National Study of Americans' Reactions to September 11

Schlenger WE, Caddell JM, Ebert L, et al.

Background: The exposure to trauma brought about by the terrorist attacks of September 11, 2001, was unprecedented in the United States. This study sought to assess levels of symptoms of posttraumatic stress disorder (PTSD) and clinically significant psychological distress following the attacks and to explore how postattack symptoms were associated with factors related to exposure. **Method:** In a Web-based epidemiological survey of a nationally representative cross-sectional sample of 2273 adults, including oversamples of the New York, N.Y., and Washington, D.C., metropolitan areas, trauma-related symptoms were measured using the PTSD Checklist and the Brief Symptom Inventory, which were administered 1 to 2 months after the attacks. In addition to self-report of symptoms by adults, the study also included adult reports of distress symptoms among children living in their households. **Results:** Of all areas studies, the New York City metropolitan area had the highest prevalence of probable PTSD (11.2%), a level significantly higher ($p = .007$) than those found in Washington, D.C. (2.7%), other major metropolitan areas (3.6%), and the rest of the country (4.0%). Overall levels of distress across the United States, however, were within expected ranges for a general community sample when determined using a broader measure of clinically important psychological distress. In multivariate models, PTSD symptom levels were associated with sex, age, direct exposure to the attacks, and time spent watching television coverage of the attacks on and during the days immediately after September 11. More broadly defined dis-

tress was associated with sex, number of hours of television coverage watched, and index of the content of that television coverage. In New York City, more than 60% of adults in households with children reported that at least 1 child in the household was upset by the attacks. **Conclusions:** Probable PTSD was associated with direct exposure to the September 11 terrorist attacks among adults 1 to 2 months after the attacks occurred, with the prevalence significantly higher in the New York City metropolitan area than elsewhere in the country. Overall levels of distress in the country, however, were within normal ranges. The course of symptoms and recovery among adults and the types and severity of distress in children in the wake of the September 11 terrorist attacks should be documented in future research.

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Sex Differences in Depressed Substance Abusers

Sinha R, Rounsaville BJ

Objective: The main goal of this article is to highlight gender-specific differences in the epidemiology, clinical nature, and treatment responses of comorbid depression and substance abuse. The second goal is to make recommendations for future research in the area of gender-specific aspects of comorbid depression and substance abuse. **Data Synthesis:** A literature review was conducted using the keywords *sex*, *gender*, *depression*, and *substance use disorders* for the time period 1980 to the present. We first outline the well-known sex differences in the epidemiology of depressed substance abusers and discuss the clinical significance of substance abuse in depression. Two distinct ways of understanding the role of substance abuse in depression are presented. The first is the role that depression may play in escalation of substance use, and the second is depression as a common sequela of chronic substance abuse. These 2 manifestations that are not mutually exclusive, often co-occurring in female substance abusers, have important treatment implications. Research on treatment response for the above clinical presentations is discussed followed by a summary of the factors that may influence sex differences in the association between depression and substance abuse. **Conclusion:** Recommendations for future research examining sex differences in animal models of depression, substance abuse, and therapeutic response to medications were made. The need for gender-specific clinical research on the association between depression, stress, and substance abuse is also highlighted.

(*J Clin Psychiatry* 2002;63:616–627)

Risperidone in Children With Autism and Serious Behavioral Problems

Research Units on Pediatric Psychopharmacology
Autism Network

Background: Atypical antipsychotic agents, unlike traditional antipsychotic medications, block postsynaptic serotonin receptors as well as dopamine receptors and thus are associated with a lower frequency of extrapyramidal side effects than are the tra-

ditional agents. This lower side effect burden, combined with efficacy for treating both positive and negative symptoms in adults with schizophrenia, suggests that the atypical antipsychotics may be beneficial in autistic children with serious behavioral disturbances. Data on the efficacy and safety of these agents in children, however, are limited. **Method:** In this multisite, double-blind, randomized trial, risperidone was compared with placebo for treatment of DSM-IV autistic disorder associated with severe tantrums, aggression, or self-injurious behavior in children aged 5 to 17 years. Scores on the Irritability subscale of the Aberrant Behavior Checklist and the Clinical Global Impressions-Improvement scale CGI-I at 8 weeks were the primary outcome measures. Positive response was defined as a $\geq 25\%$ decrease in the Irritability score and a CGI-I rating of much or very much improved. **Results:** The study sample included 101 children (82 boys and 19 girls; mean \pm SD age = 8.8 ± 2.7 years); 49 were randomly assigned to treatment with risperidone, and 52, to placebo. After 8 weeks, risperidone treatment (dose range, 0.5–3.5 mg/day) led to a 56.9% reduction in the Irritability score, compared with a 14.1% decrease found with placebo ($p < .001$). The rate of positive response was 69% (34/49) in the risperidone group and 12% (6/52) in the placebo group ($p < .001$). The average weight gain with risperidone was 2.7 ± 2.9 kg, as compared with 0.8 ± 2.2 kg with placebo ($p < .001$). Side effects that were more common ($p < .05$ for each) with risperidone than with placebo were increased appetite, fatigue, drowsiness, dizziness, and drooling. The benefit of risperidone was maintained at 6 months for 23 of the 34 children who had a positive response at 8 weeks. **Conclusions:** In autistic children, risperidone was effective and well tolerated in the treatment of tantrums, aggression, or self-injurious behavior. Inferences about adverse effects such as tardive dyskinesia are limited by the short duration of this trial.

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The Pharmacologic Treatment of Depression: Is Gender a Critical Factor?

Yonkers KA, Brawman-Mintzer O

Background: In the medical literature, there is a lack of sex-specific information regarding the efficacy, metabolism, and side effects associated with psychopharmacologic treatment. In part, this lack results from the historic underinclusion of women in clinical trials during early drug development, but it also occurs because investigators of treatment and metabolic studies do not routinely analyze results according to sex. In 1993, the U.S. Food and Drug Administration (FDA) announced changes that encourage the inclusion of women in early pharmacokinetic studies and emphasize the need for subset analyses using sex and age parameters. In conjunction with advances in basic science regarding drug metabolism, these modifications have led to modest increases in information regarding sex differences in drug metabolism and efficacy. In this article, current information regarding potential sex differences in the pharmacotherapy of major depressive disorder is reviewed. **Data Sources:** A MEDLINE search was conducted using the terms *antidepressants*, *sex-factors*, *gender differences*, and *women* for the years 1966 to 2000. **Data Synthesis and Conclusions:** There are data supporting sex differences in the activity of various antidepressant-metabolizing enzymes. However, there is a paucity of investigation regarding how these differences might translate into differences in clinical efficacy. Notably, there is little work using existing databases to perform the subgroup analyses recommended by the FDA. The widespread dissemination of such work is needed, and, if conducted, investigations in this area have the potential to enhance psychopharmacologic treatment for both men and women.

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